Notice of Allowability	Application No.	Applicant(s)	
	10/705,743	ZHAO ET AL.	
	Examiner	Art Unit	
	Thomas S. Heard	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *Exam amendment, June 20, 2007*.

2. ☒ The allowed claim(s) is/are *1-7,9,10,16 and 36-39*.

3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☒ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application
6. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____ .
7. ☒ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

6/14/07
ANISH GUPTA
PRIMARY EXAMINER

EXAMINER'S AMENDMENT

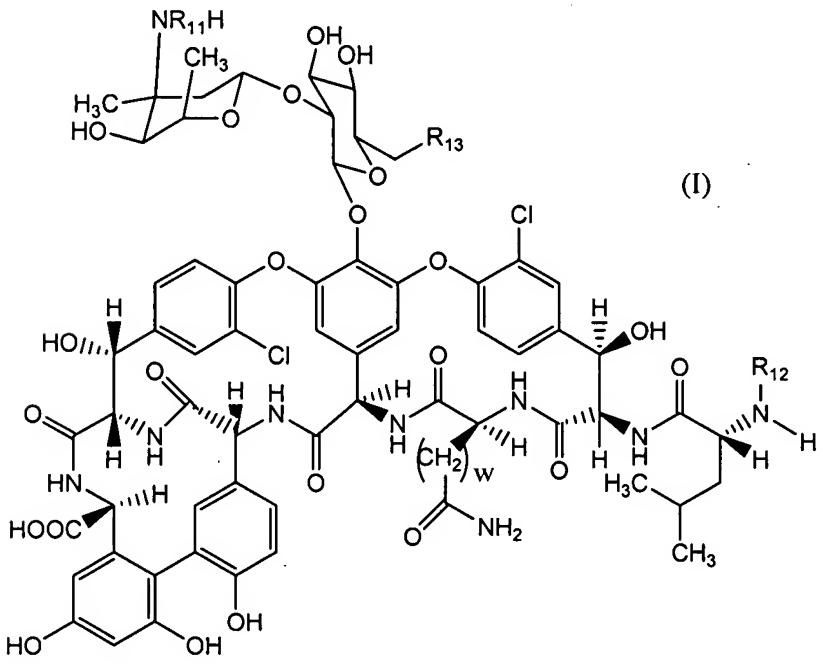
An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Hyun Soon Cho (Recognition No. L0306) and Michael Mercanti Reg No. 33,966 (Attorney) on June 20, 2007.

The application has been amended as follows:

1. (Currently Amended) A method of preparing a vancomycin-polymer conjugate wherein the polymer is conjugated to the sugar amino group of a vancomycin, comprising:

reacting a vancomycin compound of the formula:



(I)

wherein

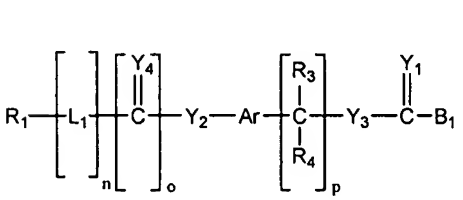
R_{11} and R_{12} are independently selected from the group consisting of hydrogen, C_{1-6} alkyl[s], C_{3-12} branched alkyl[s], C_{3-8} cycloalkyl[s], C_{1-6} substituted alkyl[s], C_{3-8} substituted cycloalkyl[s], aryl[s], substituted aryl[s], aralkyl[s], C_{1-6} heteroalkyl[s], substituted C_{1-6} heteroalkyl[s], C_{1-6} alkoxyalkyl, phenoxyalkyl and C_{1-6} heteroalkoxy[s];

R_{13} is OH, NH-aryl, NH-aralkyl, or NH-C_{1-12} alkyl; and

w is 1 or 2;

in the presence of at least about a ten-fold molar excess of triethylamine and a sufficient amount of dimethylformamide with a polyalkylene oxide ~~polymer~~ residue containing at least one leaving group ~~capable of reacting~~ that reacts with the sugar amino group $NR_{11}H$ of said vancomycin compound ~~in the presence of at least about a ten-fold molar excess of triethylamine and a sufficient amount of dimethylformamide~~.

2. (Currently Amended) The method of claim 1, wherein said ~~activated~~ polyalkylene oxide ~~polymer~~ residue is activated, and wherein the said activated polyalkylene oxide residue is selected from the group consisting of:



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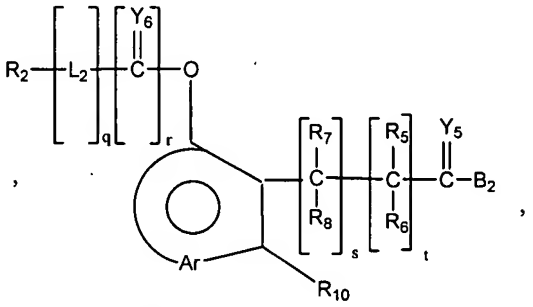

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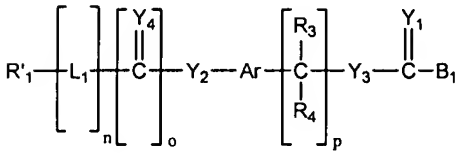

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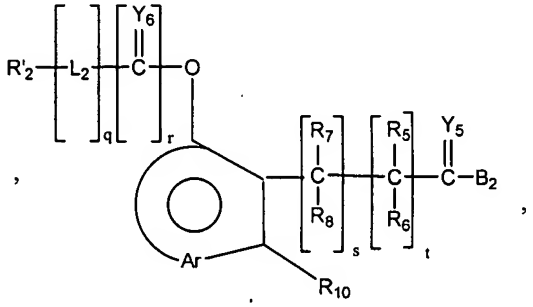

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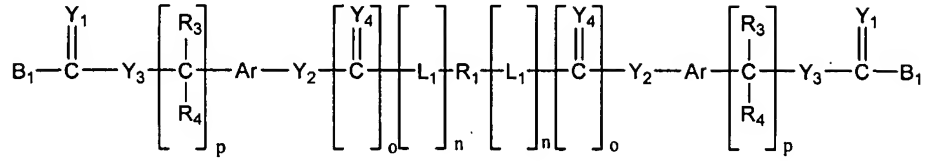
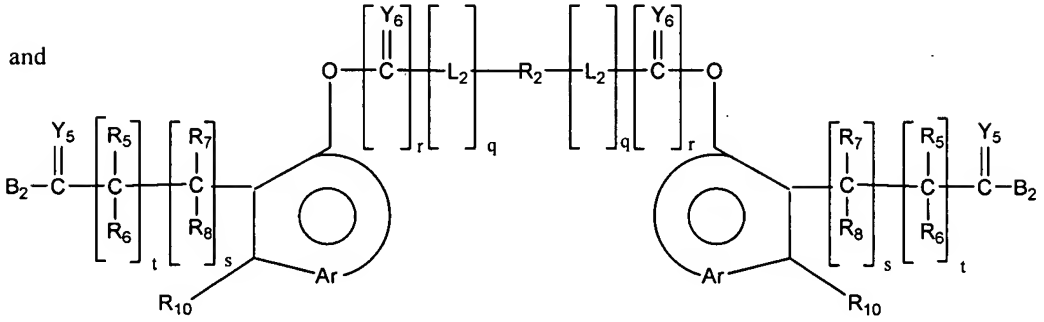


and



wherein:

R_1 and R_2 are independently selected <u>from polyalkylene oxide</u> ~~polymer~~ residues;

<u>R'_1 and R'_2 are independently selected from branched polyalkylene oxide residues;</u>

Y_{1-6} are independently selected from the group consisting of O, S or NR_9;

R_{3-10} are independently selected from the group consisting of hydrogen, <u>C_{1-6} alkyl,</u>

<u>C_{3-12} branched alkyl, C_{3-8} cycloalkyl, C_{1-6} substituted alkyl, C_{3-8} substituted cyloalkyl, aryl, substituted aryl, aralkyl, C_{1-6} heteroalkyl, substituted C_{1-6} heteroalkyl, C_{1-6} alkoxyalkyl, phenoxyalkyl and C_{1-6} heteroalkoxy</u> ~~C_{1-6} alkyls, C_{3-12} branched alkyls, C_{3-8} cycloalkyls, C_{1-6} substituted alkyls, C_{3-8} substituted cyloalkyls, aryls, substituted aryls, aralkyls, C_{1-6} heteroalkyls, substituted C_{1-6} heteroalkyls, C_{1-6} alkoxyalkyl, phenoxyalkyl and C_{1-6} heteroalkoxys~~;

Ar is a moiety which forms a multi-substituted aromatic hydrocarbon or a multi-substituted heterocyclic group;

L_1 and L_2 are independently selected <u>from</u> bifunctional linkers;

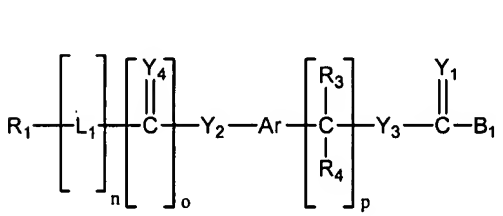
B_1 and B_2 are independently selected <u>from</u> leaving groups;

p and t are independently selected from positive integers;

n, q and s are independently either zero or a positive integer; and

o and r are independently zero or one.

3. (Currently Amended) The method of claim 2, wherein said activated polyalkylene oxide ~~polymer~~ residue is selected from the group consisting of



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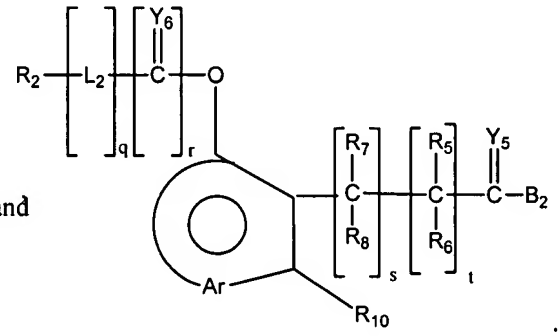
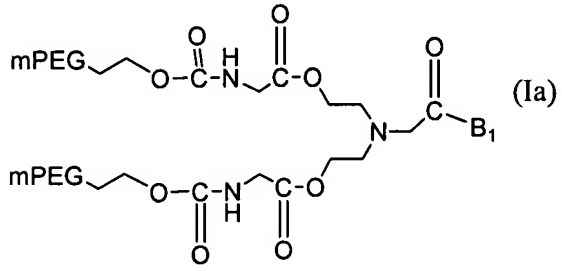


4. (Currently Amended) The method of claim 1, wherein said ~~activated~~ polyalkylene oxide ~~polymer~~ residue is activated, and wherein said activated polyalkylene oxide is selected from the group consisting of:



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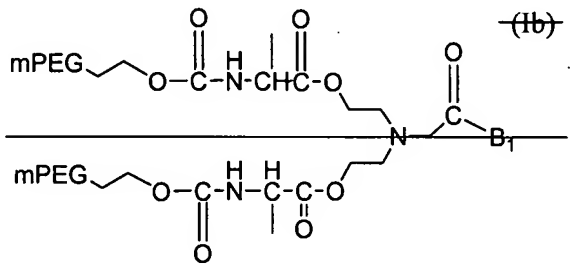
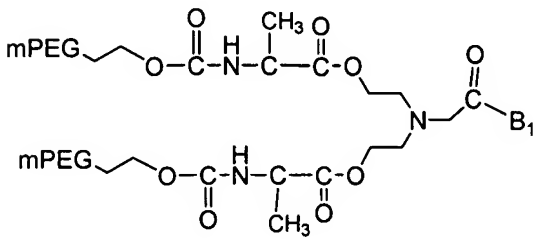
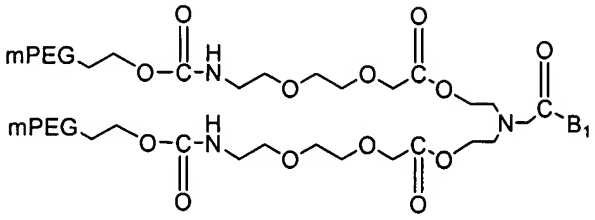


~~(Ib)~~



(Ib)



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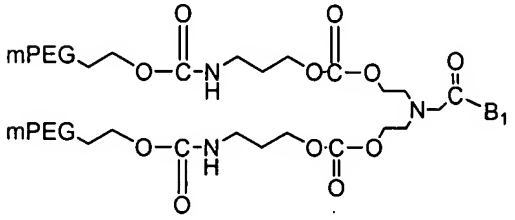

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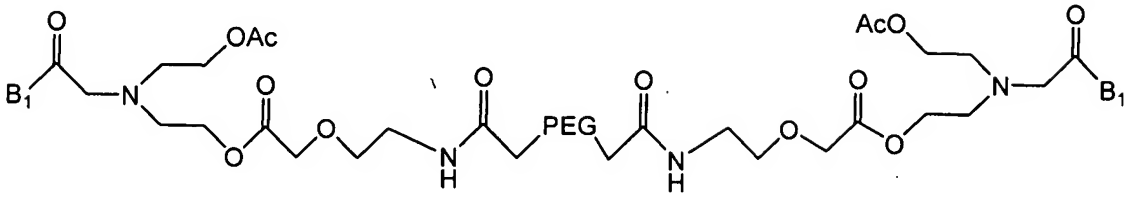

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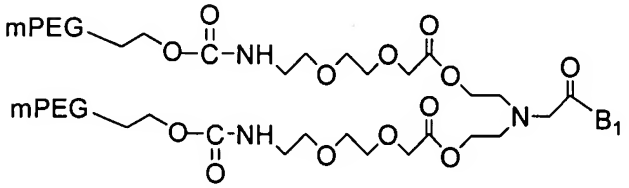
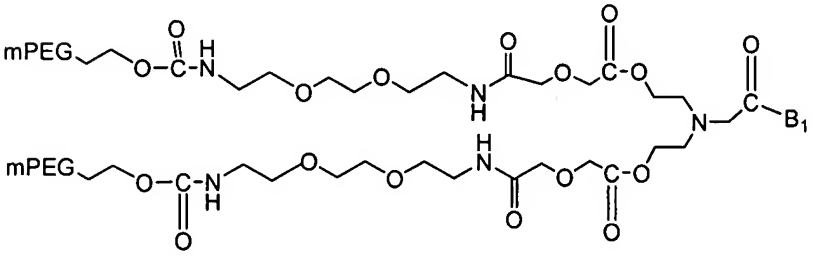


(If)



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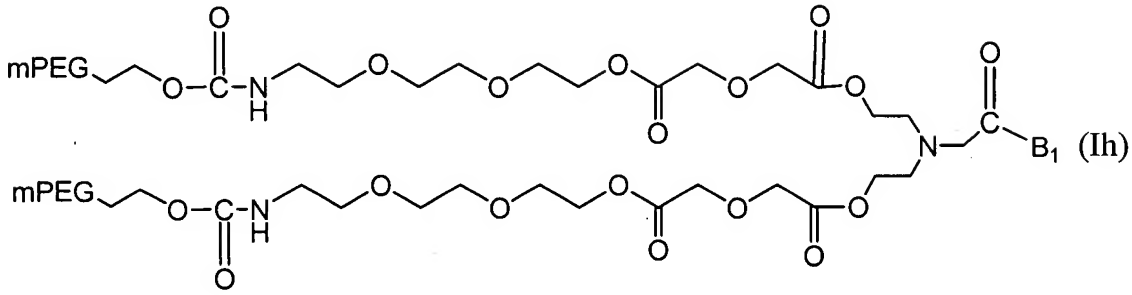
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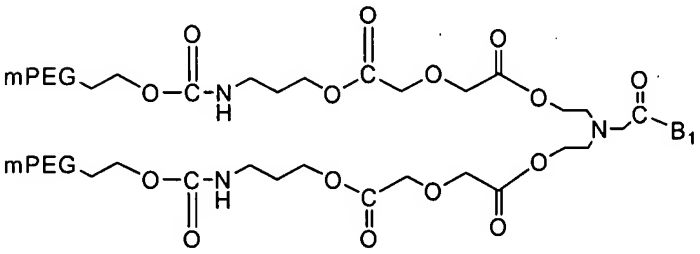
mPEG
B1

(Ih)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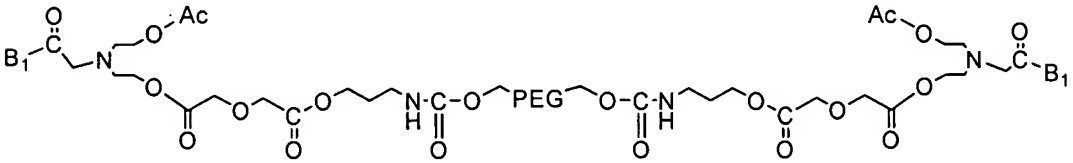
(Ii)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Ac
Ac
B1
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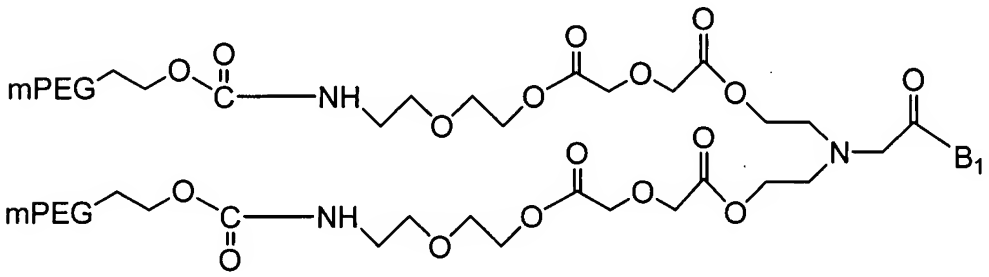
(Ij)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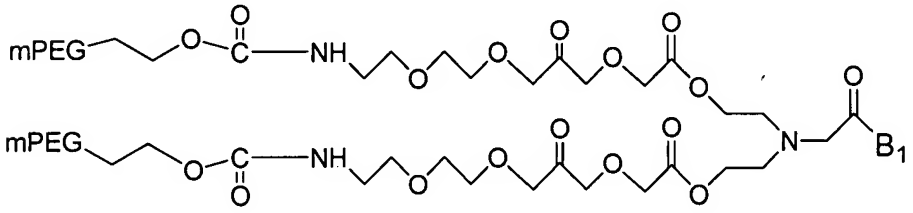
(Ik)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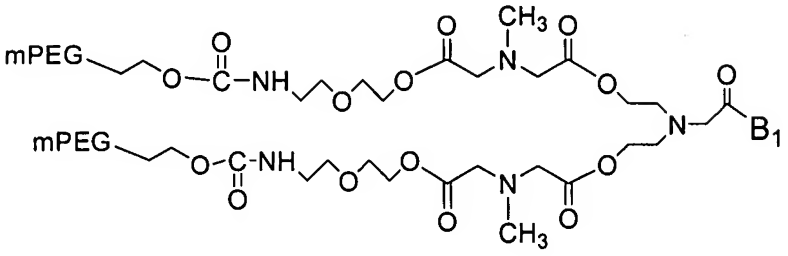
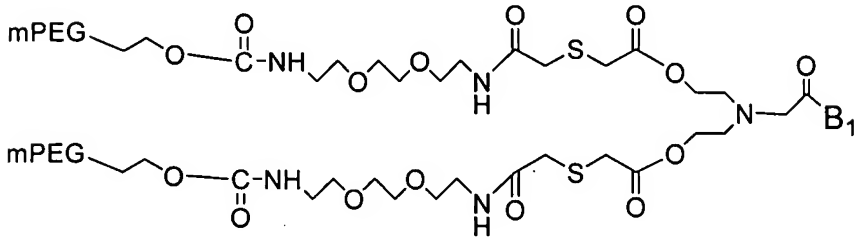
(Il)



(Im)



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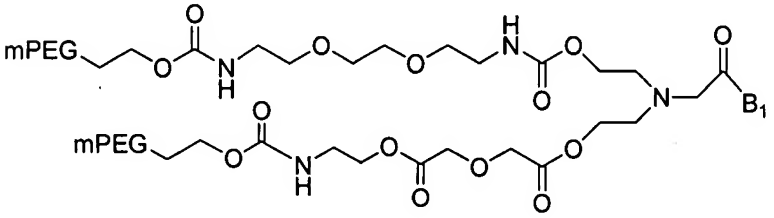

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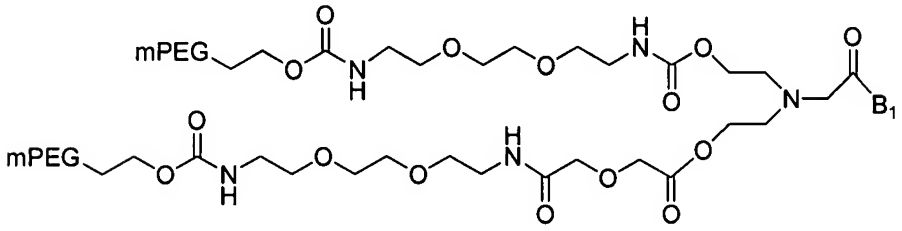

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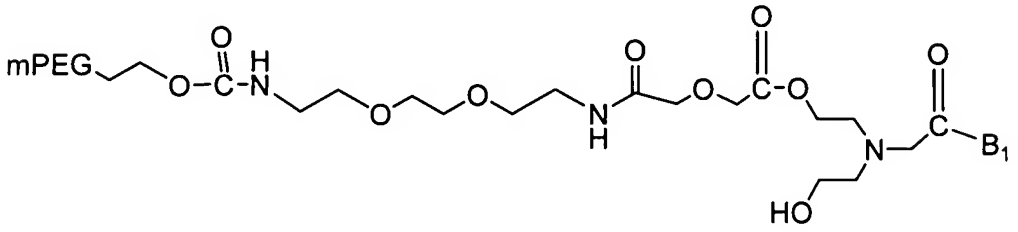
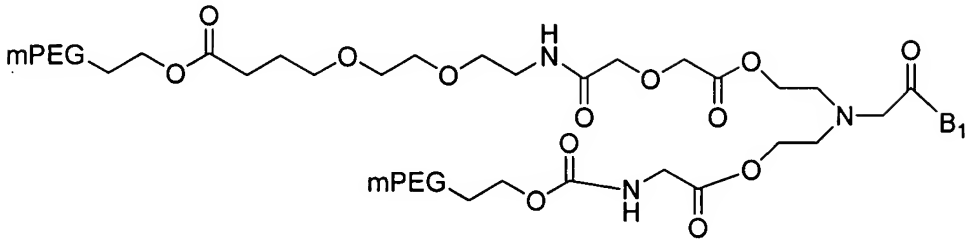
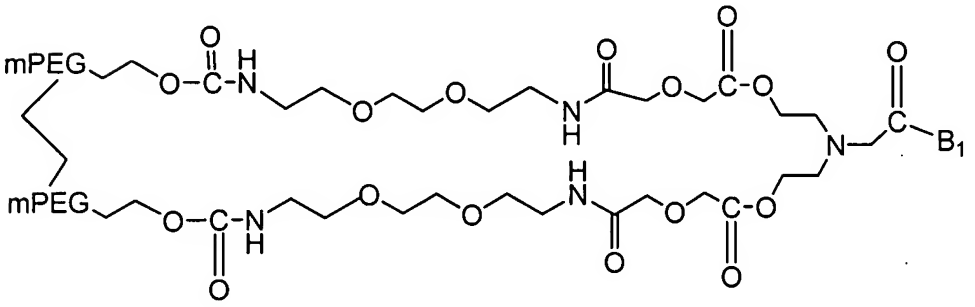


(Iq)

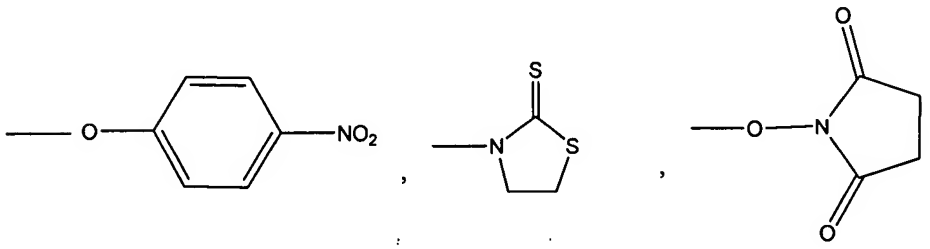


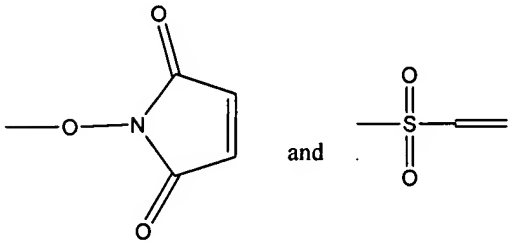
(Ir)



(Is)

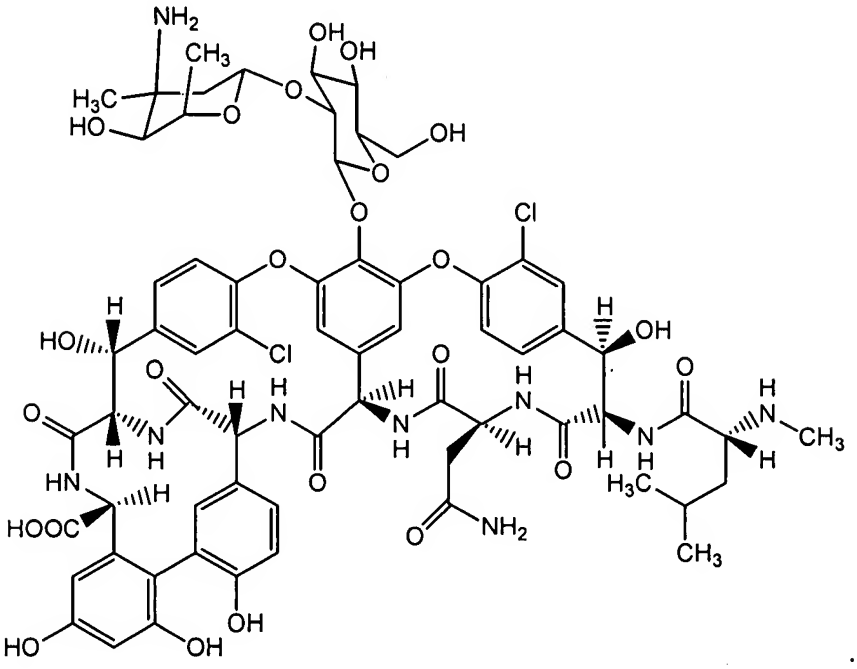
wherein B_1 is selected from the group consisting of:



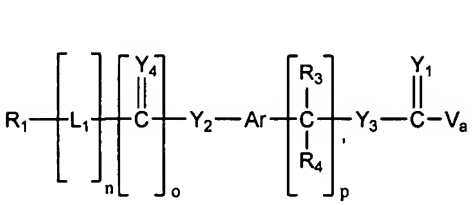


and

5. (Original) The method of claim 1, wherein said vancomycin compound is:



6. (Currently Amended) The method of claim 2, wherein said vancomycin polymer conjugate is selected from the group consisting of



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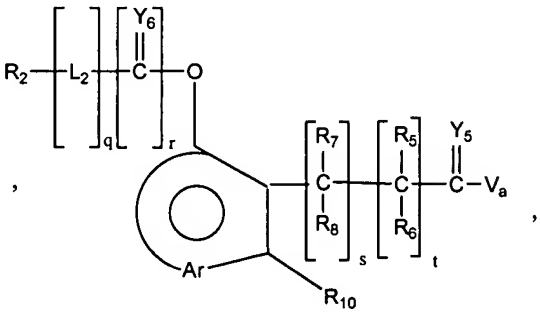

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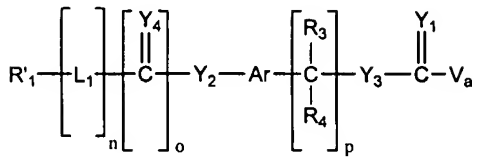

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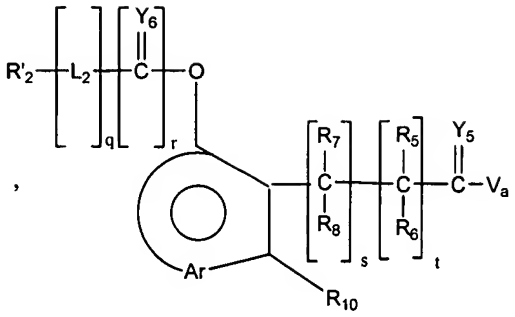

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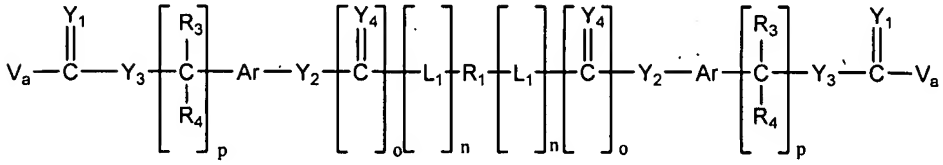
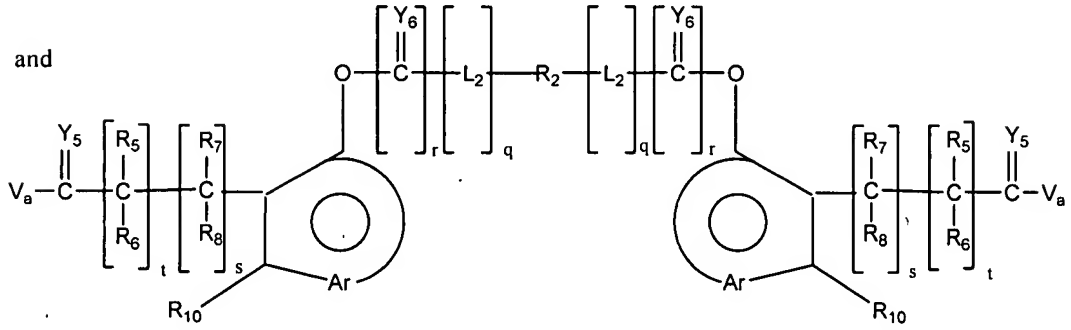
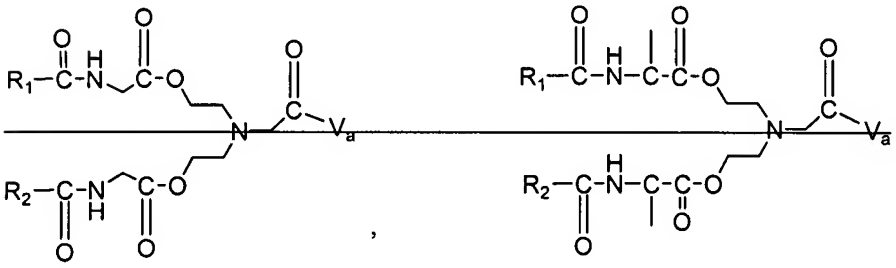


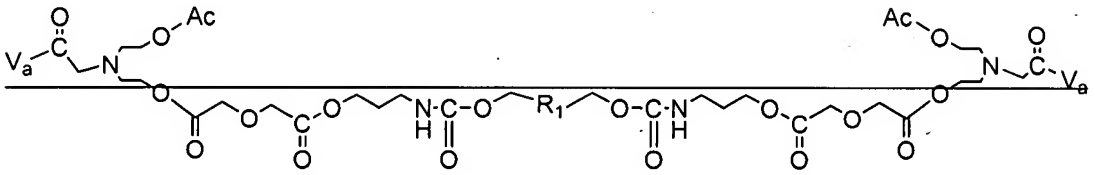
and



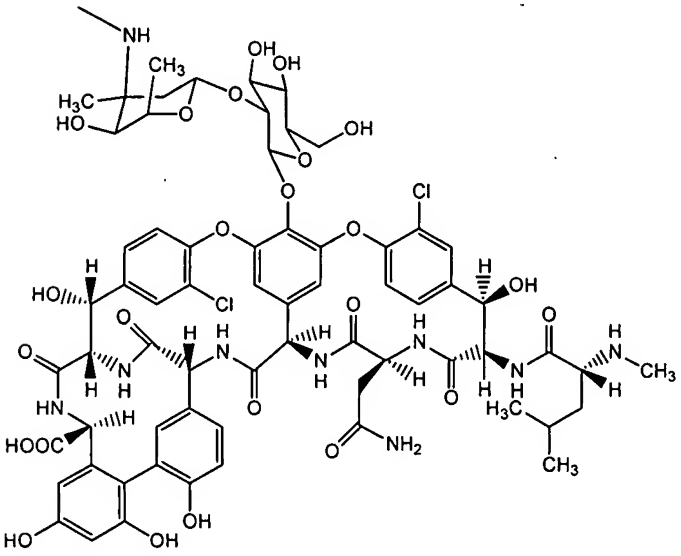


,

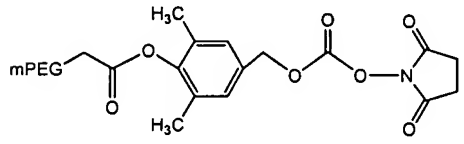
~~and~~

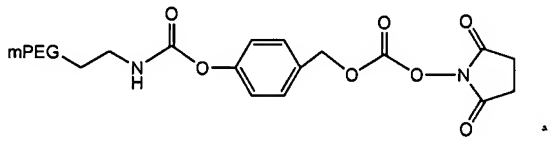


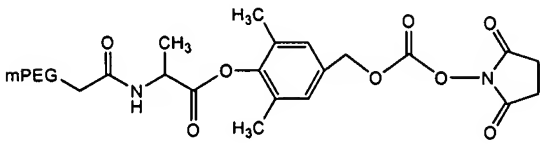
wherein V_a is

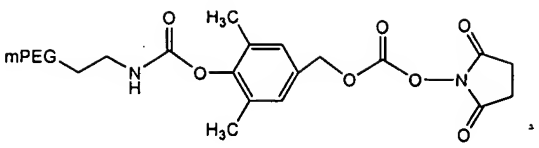


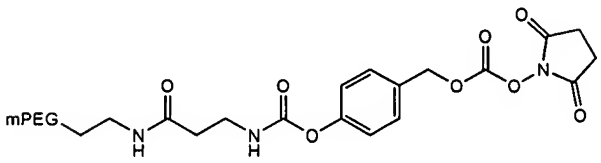
7. (Currently Amended) The method of claim 1, wherein said polyalkylene oxide ~~polymer~~ containing said leaving group is selected from the group consisting of

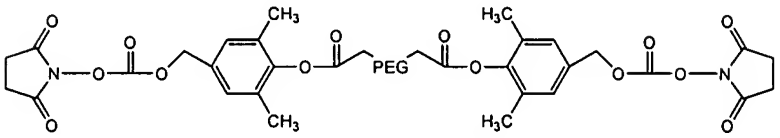


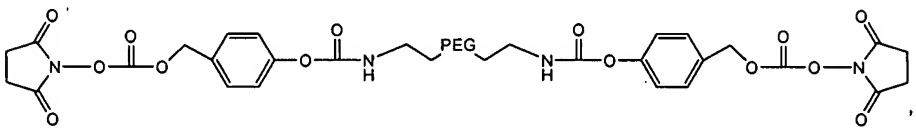


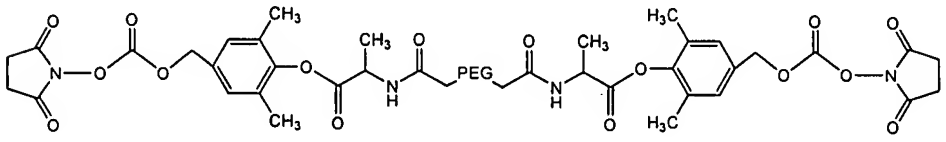


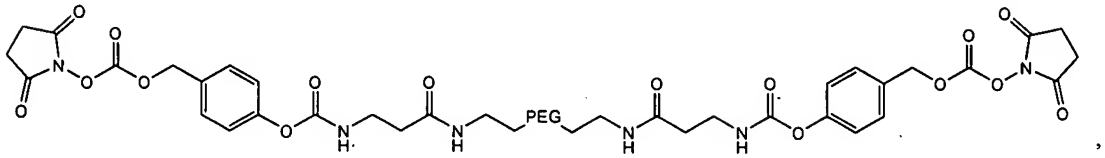


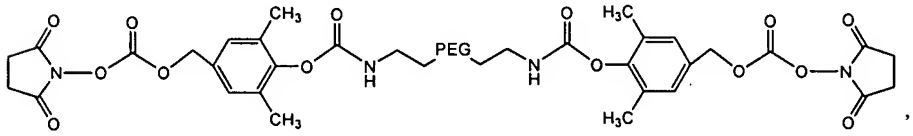


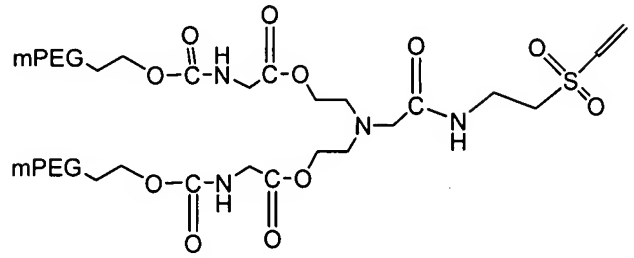












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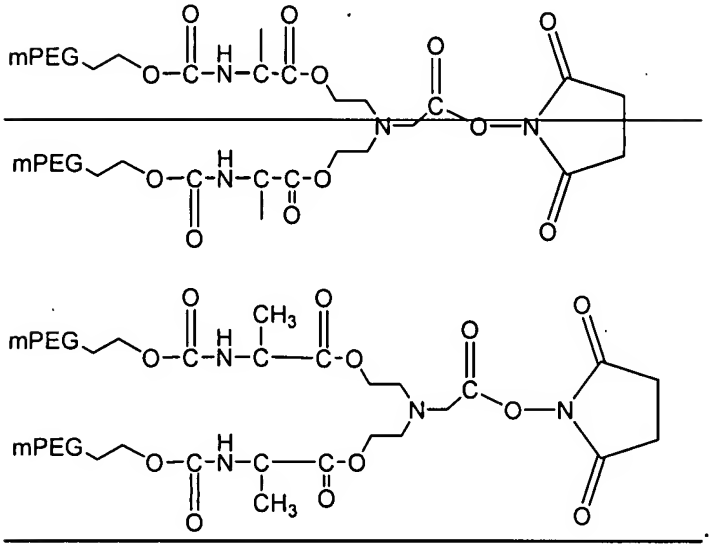
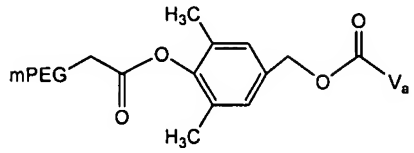
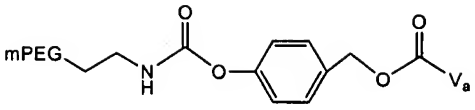


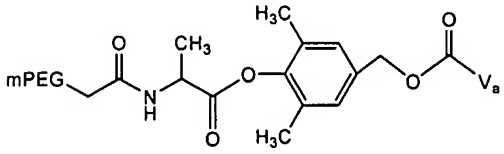
8. (Cancelled)

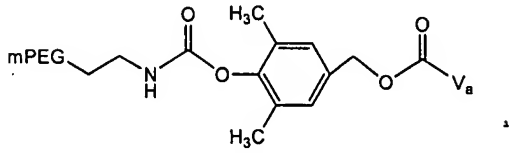
9. (Currently Amended) The method of claim 2, wherein R_1 and R_2 are independently selected from polyethylene glycol residues and R'_1 and R'_2 are independently selected from branched polyethylene glycol residues.

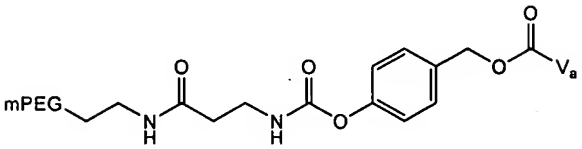
10. (Currently Amended) The method of claim 1, wherein said vancomycin-polymer conjugate is selected from the group consisting of

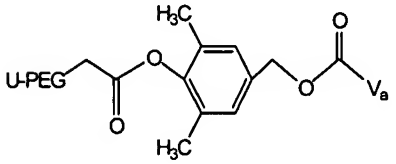


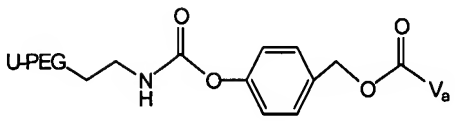


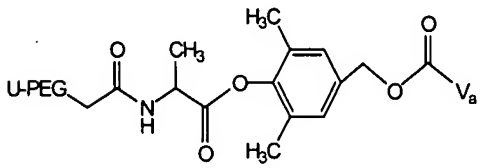


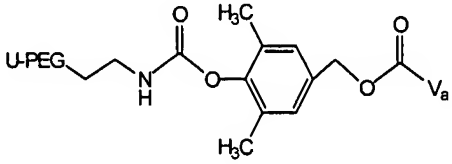


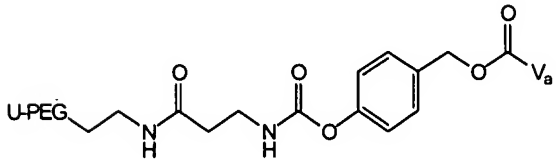


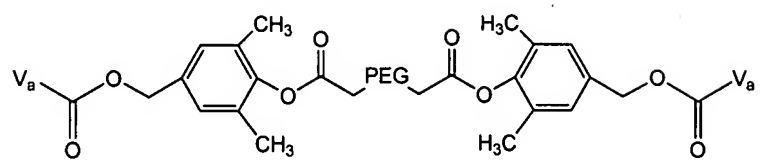


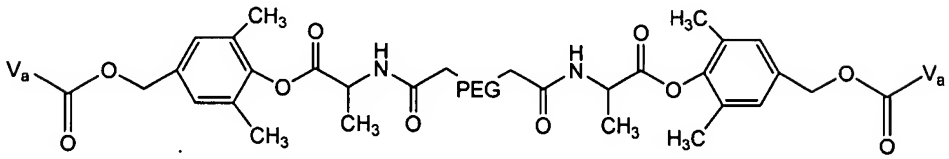


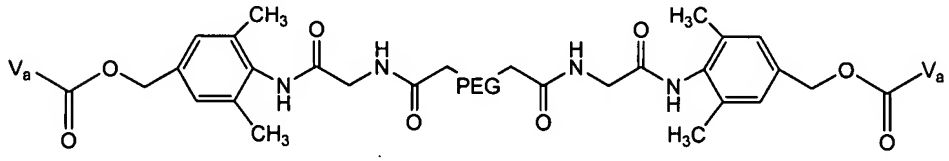


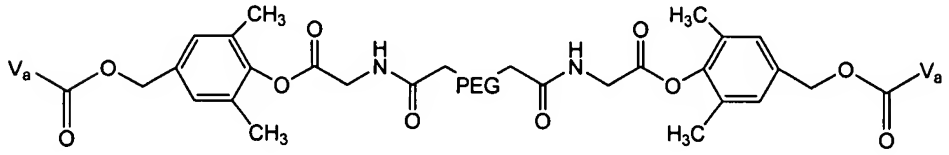


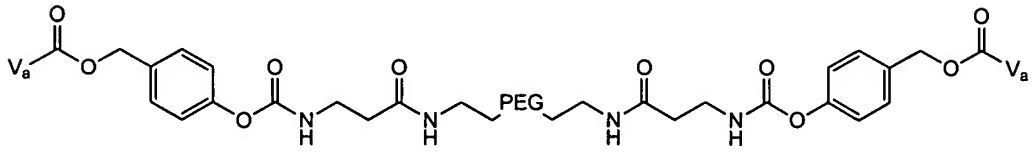


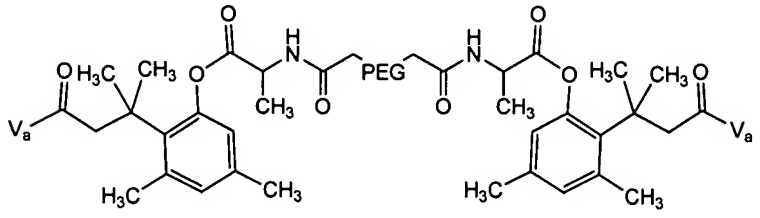


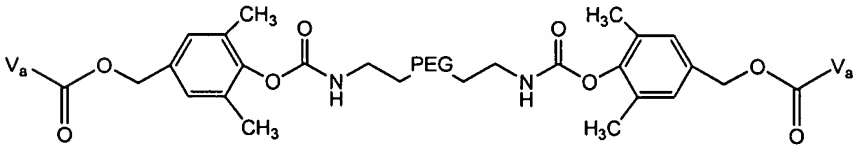


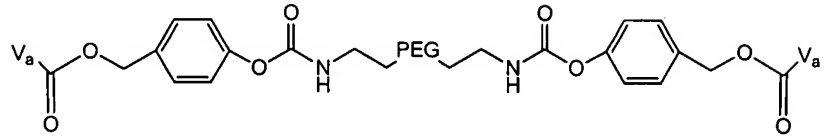


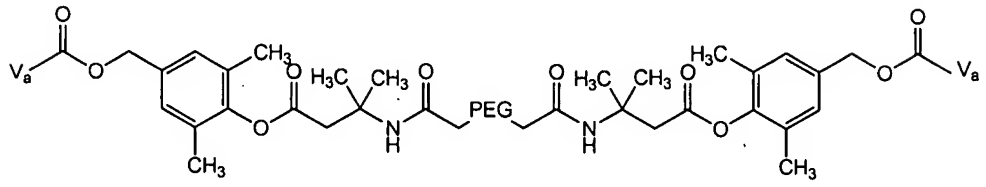


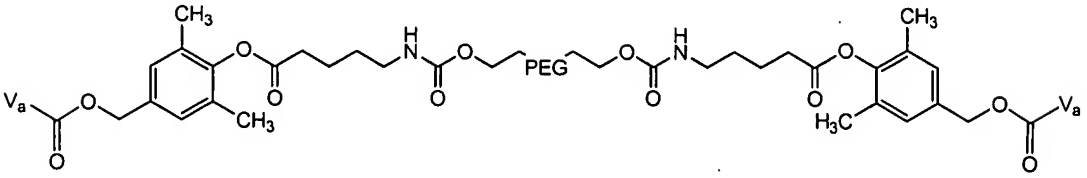


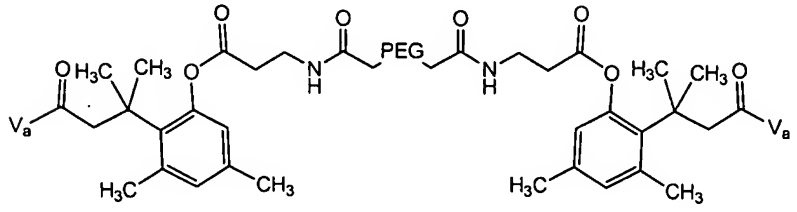


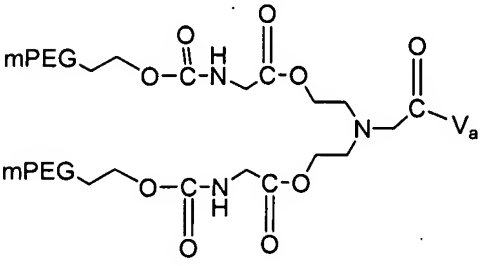


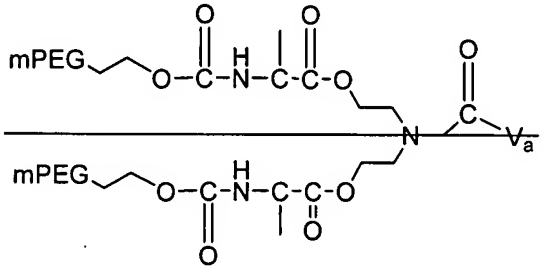


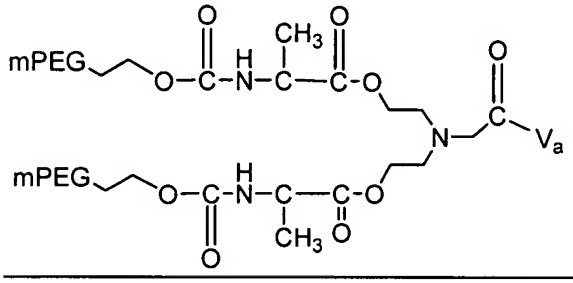












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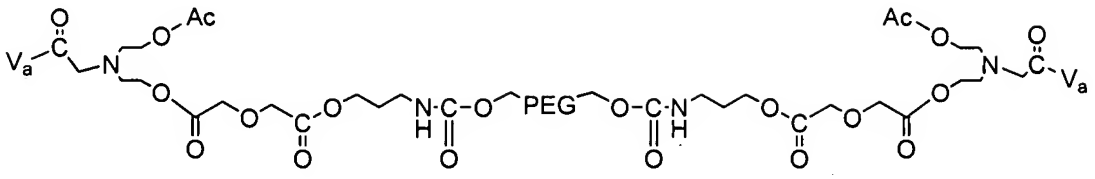


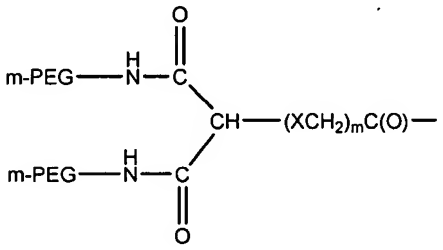
wherein

PEG is $-O(-CH_2CH_2O)_x-$;

mPEG is $H_3CO(-CH_2CH_2O)_x-$;

x is a positive integer selected from about 10 to about 2300, and

U-PEG is selected from the group consisting of



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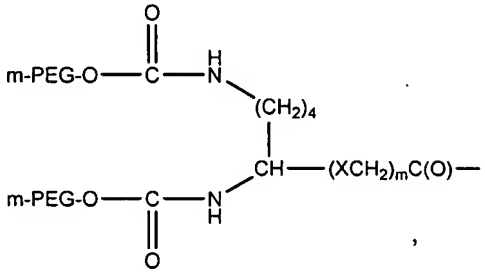

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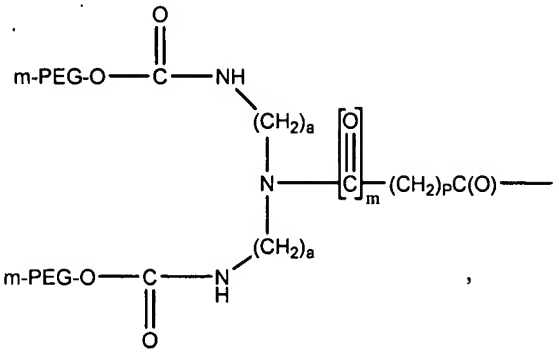

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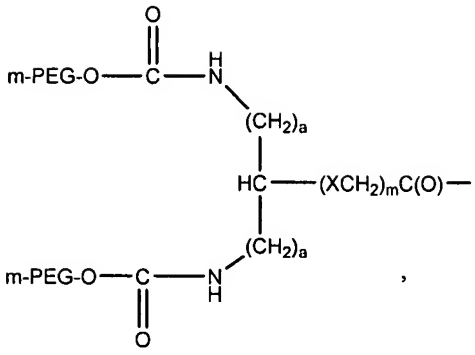

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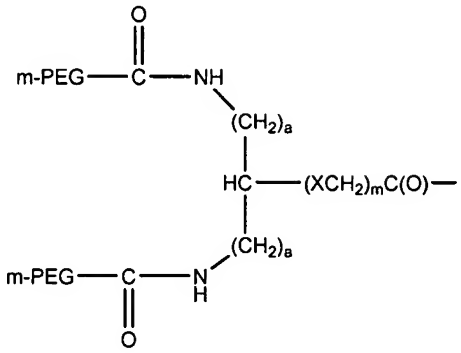
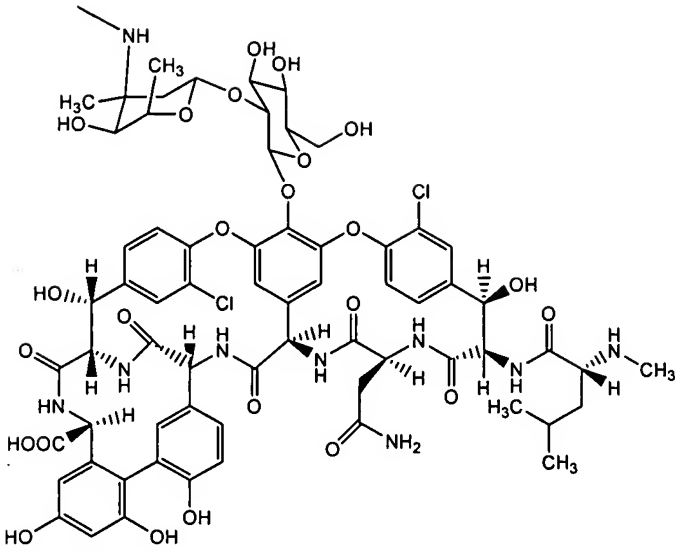


V_a is



11-15. (Cancelled)

16. (Original) The method of claim 1, wherein said molar excess of triethylamine is at least about 30-fold.

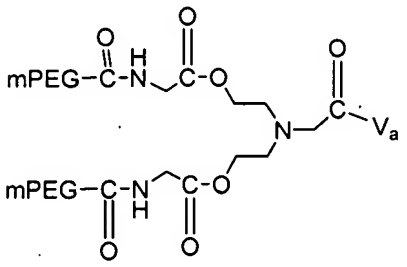
17-35. (Cancelled)

36. (New) The method of claim 1, wherein said molar excess of triethylamine is at least about 20-fold.

37. (New) The method of claim 1, wherein said sufficient amount of dimethylformamide ranges from about 10 ml/g vancomycin to about 500 ml/g vancomycin.

38. (New) The method of claim 1, wherein said sufficient amount of dimethylformamide ranges from about 100 ml/g vancomycin to about 200 ml/g vancomycin.

39. (New) The method of claim 4, wherein said vancomycin polymer conjugate is selected from the group consisting of



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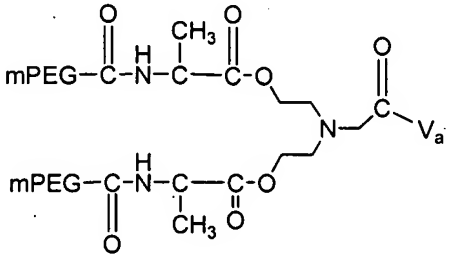

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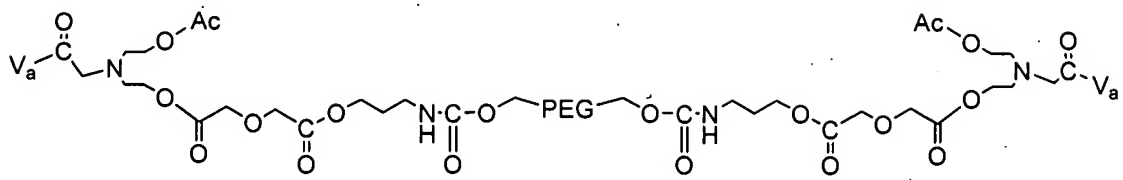
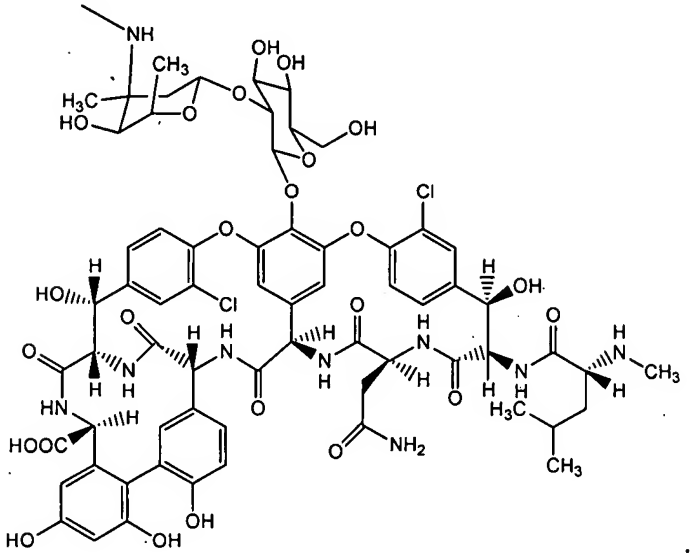


wherein V_a is



The following is an examiner's statement of reasons for allowance: The instantly claimed invention is drawn to vancomycin conjugates to polyalkylene oxide polymer residues. The closest prior art is Martinez, et al, US 6,395,266. Martinez et al discloses terminally-branched polymeric linkers and polymeric conjugates of a number of drug, such as vancomycin, instantly claimed. However, Martinez neither teaches nor suggests the specific solvent/base requirements of triethylamine and

dimethylformamide to couple the polymers specifically at $NR_{11}H$, nor does Martinez teach or suggest the linkers and conjugates instantly claimed.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Conclusion

Claims 1-7, 9, 10, 16, 36-39 are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Thomas S. Heard whose telephone number is (571) 272-2064. The examiner can normally be reached on 9:00 a.m. to 6:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on (571) 272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should

you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

TSH